REMARKS

Claims 13-17, 20-38 and 40-52 are pending and stand ready for further action on the merits. Claims 13-17, 20-22, 24-38 have been amended for clarity. New claims 41-50 find support at pages 2-3 of the specification. Support for new claim 51 can be found at page 9, paragraphs 1-3 and in examples 1 and 2. Support for new claim 52 can be found in claim 27.

The specification has been amended to improve clarity. No new matter has been added by way of the above-amendment.

PRIOR ART BASED ISSUES

Claims 1-12, 13, 14, 17, 19, 20, 21, 22, 33 and 40 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Derwent Abstract 1995-228634 (hereinafter Derwent '634) further in view of JP 7-138180 or Ramsewak et al. 1999:38735 (Abstract). Applicants respectfully traverse the rejection.

Advantages of the Present Invention

It is currently accepted in the anti-asthma art that leukotrienes are biological mediators of asthma and the oxidation of arachidonic acid is the rate-determining step for the synthesis of the leukotrienes. As such, a strategy for asthma drug development is to search for, or synthesize compounds that inhibit the synthesis of leukotrienes and that will inhibit the oxidation of arachidonic acid.

The present inventors have surprisingly found that an extract composition of the plant Murraya koenigii not only inhibits the oxidation of arachidonic acid but is expected to be free of toxicity and is compatible for use in humans as the plant leaves are extensively used as food ingredients.

The results in the following table 1 (obtained from page 10 of the specification) illustrate that the active factors in the *Murraya koenigii* leaf act as an inhibitor of oxygen consumption in the presence of normal as well as activated human neutrophil and arachidonic acid. The present inventors hypothesize that the oxidation of arachidonic acid is strongly inhibited by the active factors present in the extract from the *Murraya koenigii* plant.

Table 1

Inhibition of armachidonic acid oxidation by neutrophil

Treatment	Micromole oxygen consumed/10 min	% of inhibition of O_2 consumption by active material with respect to	
		Stimulation	Without stimulation
A. Phosphate Buffered Saline for 60 min.	16.08	NA	--
B. Active extract 60 min in Phosphate Buffered Saline	12.85	--	20
C. Phorbol Myristic Acetate for 30 min.	39.58	--	
D. Calcium ionophore for 30 min.	64.01	--	
E. Active extract 30min + PMA 30 min.	21.42	46	
F. Active extract 30min.+Calcium ionophore 30 min.	25.3	60	

The above-explanation has been provided to highlight the distinctions between the present invention and the cited references.

Derwent '634 and JP '180 (hereinafter collectively JP '180)

JP '180 suggests the use of an extract from at least one plant selected from Azadirachta indica, Cymbopogon nardus, Sphaeranthus indicus, Ocimum sanctum, Tinospora cordifolia,

Murraya koenigii and Phyllanthus nuriri.

These extracts are used in a topical composition to retain the skin moisture by inhibiting the decomposition of hyaluronic acid by the enzyme hyaluronidase inhibitor.

The extract is taught to be prepared with ethanol and is mixed with additives which are typically found in skin ointments.

Applicants respectfully submit that the inventive composition claims are patentable over JP '180 for the following reasons.

According to U.S. practice, a preamble reciting an intended use is not given patentable weight unless the preamble breathes life and meaning into the claim. In other words, if the claimed product or composition can be said to be physically modified based on the intended use of the preamble, then the preamble is to be given patentable weight. According to MPEP 2111.02, any "terminology in the preamble that limits the structure of the claimed invention must be treated as a claim limitation." In the presently claimed composition, the pharmaceutical composition is used in the treatment of asthma. This in distinction to the composition of JP '180 which is useful as a skin ointment. Accordingly, the inventive pharmaceutical composition must have a distinct composition from the skin ointment composition of JP '180, particularly with respect to the pharmaceutically acceptable additives of the different composition. Thus, the present composition clearly is patentable over the composition of JP '180.

Ramsewak et al.

Ramsewak et al. teach the extraction of fresh *M. koenigii* leaves with acetone to obtain **isolated** samples of mahaninbine, murrayanol and mahanine. Ramsewak et al. do not teach or suggest any use of the extract other than to isolate these three samples.

In a step in the process of isolating these three samples, Ramsewak et al. prepare an extract of *M. koenigii* leaves with acetone. However, this extract of Ramsewak et al. is distinct from the inventive extract composition, since acetone is not a pharmaceutically acceptable additive. Accordingly, Applicants respectfully submit that the inventive composition of claim 13 is neither anticipated nor made obvious by Ramsewak et al.

Process Claims 41-50

Applicants respectively submit that the inventive process claims 41-50 which use hydrocarbon, chlorinated hydrocarbon, ether or ester solvents to obtain the extract are patentable over the teachings of Ramsewak et al. and JP '180. Ramsewak et al. use acetone to obtain the extract whereas the inventive process. Also, JP '180 use ethanol to obtain the abstract. As such, significant patentable distinctions exist between the present process claims and the teachings of Ramsewak et al. and JP '180.

In view of the foregoing, Applicants respectfully request withdrawal of the prior art based rejection.

Issues Related to the Phrases "extract" and "pharmaceutically acceptable additive"

In view of the phrases "extract" and "pharmaceutically acceptable additive", the Examiner has rejected certain claims: A) under 35 U.S.C. §112, first paragraph for lacking sufficient written description support; B) under 35 U.S.C. §112, first paragraph for not being enabled; and C) under 35 U.S.C. §112, second paragraph for being indefinite. Applicants respectfully traverse each of the rejections.

With regard to the term "extract", the Examiner appears to be requiring that each component of the extract be isolated and identified. Applicants respectfully submit that all that is required, is that the skilled artisan would be able to make the extract as presently claimed. In the present specification at page 7, the skilled artisan is shown in steps (1)-(6) how to prepare the extract. Also, in Examples 1-3 on pages 8-9, the skilled artisan is provided with a specific "cook book recipe" for preparing the extract. Accordingly, Applicants respectfully submit that the present specification has placed the inventive "extract" in the possession of the public.

The Examiner has made similar objections to the phrase "pharmaceutically acceptable additive". First, Applicants respectfully submit that the present specification, at page 4, line 1 to page 6, line 7 provides specific examples of what is considered to be encompassed by the term "pharmaceutically

acceptable additive." Second, Applicants respectfully submit that this phrase is often used in the art. This is shown by a word search of the USPTO Patent Full Text and Image Database, which shows that 793 patents contain this phrase in the specification when searched from the years 1976 to present. This search result is attached hereto as an appendix for the Examiner's review.

As such, the skilled artisan would be able to ascertain whether a specific compound or composition is encompassed by the phrase "pharmaceutically acceptable additive" and would be able to make the inventive composition containing these additives. As such, the inventive claims containing the phrase "pharmaceutically acceptable additive" fully meets the requirements of 35 U.S.C. §112.

In view of the foregoing, withdrawal of the rejections under 35 U.S.C. §112 are respectfully requested.

Additional Issues Under 35 U.S.C. §112, second paragraph

Claims 3, 6, 12, 14, 18, 24, 28, 30, 32, 36 and 39 are rejected under 35 U.S.C. §112, second paragraph for being indefinite. Applicants respectfully traverse the rejection.

Applicants respectfully submit that the above-amendment addresses each of the Examiner's specific objections raised (except for those described in the section above with regard to the term "extract" and the phrase "pharmaceutically acceptable additives"). As such, Applicants respectfully submit that the

claims, as presently amended, particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Withdrawal of the rejection is respectfully requested.

Issues Under 35 U.S.C. §101 and 112, second paragraph

Claims 39 is rejected under 35 U.S.C. §101 and §112, second paragraph. Applicants respectfully traverse each of the rejections.

In view of the cancellation of claim 39, these rejections are rendered moot.

Conclusion

In view of the above amendments and comments, Applicants respectfully submit that the claims are in condition for allowance. A notice to such effect is earnestly solicited.

If the Examiner has any questions concerning this application, he is requested to contact Garth M. Dahlen, Ph.D. (#43,575) at the offices of Birch, Stewart, Kolasch & Birch, LLP.

A marked up copy of the specification and claims showing changes made is attached hereto as an appendix for the Examiner's convenience.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one month to January 20, 2003 (a federal holiday) in which to file a reply to

the Office Action. **The required fee of $110.00 is to be charged to Deposit Account No. 02-2448.**

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fee required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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VERSION WITH MARKIGNS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification has been amended as follows:

Please replace the second paragraph on page 2 with the following rewritten paragraph:

--The [applicants] inventors undertook a study on the extracts of this plant to identify the therapeutic principles of the plant. During their study, the [applicants] inventors discovered the presence of the active principles in the leaf of *Murraya koenigii* which surprisingly were found to be useful in the treatment and cure of asthma.

Please replace the third paragraph on page 4 with the following rewritten paragraph:

--Further, the invention provides a method for the treatment of asthma, said method comprising the steps of administering an effective amount of the composition [as claimed in claim 13] comprising an extract obtained from the plant *Murraya koenigii* and at least one pharmaceutically acceptable additive to a subject in need thereof.

Please replace the paragraph on page 5, lines 1-3 with the following rewritten paragraph:

--In an embodiment, the lyophilized extract obtained from *Murraya Koenigii* is administered alone or [alongwith] along with

other conventional additives for the treatment of asthma. In still another embodiment, the mode of administration is oral for the treatment of mild or acute asthma.

Please replace the paragraph on page 5, lines 15-18 with the following rewritten paragraph:

--In another embodiment, the additives [obatined] obtained from *M. paniculate Linn, H. abelmoschus, T. ammi, S. aromaticum, A.vasica Nees, E hirta,* and *M. koinegii* are administered to include properties such as [antidiahorial] antidiarrheal, antiseptic, carminative, stimulation, anti-cough, anti-bronchitis and nourishment.

Please replace the third paragraph on page 6 with the following rewritten paragraph:

--As said above, the active factor(s) in *Murraya koenigii* useful for relief, treatment and cure of asthmatic problem(s), the preparation of which comprises drying, powdering, and extracting the dried leaves of the plant, *Murraya koenigii*, in a percolator at an ambient temperature using appropriate solvents and concentrating the extract under reduced pressure and finally lyophilizing the concentrate to make the active factor(s).

Please replace Table 1 beginning on page 10 with the following rewritten Table 1:

--Table 1

Inhibition of arachidonic acid oxidation by neutrophil

Treatment	Micromole oxygen consumed/10 min	% of inhibition of O_2 consumption by active material with respect to	
		Stimulation	Without stimulation
A. [PBS] Phosphate Buffered Saline for 60 min.	16.08	NA	-- 20
B. Active extract 60 min in ['1'] Phosphate Buffered Saline	12.85	--	
C. [PMA] Phorbol Myristic Acetate for 30 min.	39.58	--	
D. Calcium ionophore for 30 min.	64.01	--	
E. Active extract 30min + PMA 30 min.	21.42	46	
F. Active extract 30min.+Calcium [ionosphere] ionophore 30 min.	25.3	60	

Please replace the first paragraph on page 11 with the following rewritten paragraph:

--Calcium ionophore gave better results as there was about 60% inhibition while PMA effects 46% inhibition of [O2] O_2 consumption by active material present in *Murraya koenigii* leaf under in vitro neutrophil test. In both the stimulation

remarkable inhibition of [O2] O_2 consumption indicates the efficacy of the material.—

Please replace the fifth paragraph beginning on page 14 and ending on page 15 with the following rewritten paragraph:

--Two volunteer patients (one male and another female) with a genetic predisposition for asthma had sleepiness during night time and were very prone to asthmatic [condition for the sensitive] episodes due to sensitivity to the city pollution. Shortness of breathing was their main complain[s]t, and one [has] had to take an inhaler when [there was] a severe night attack occurred. They followed the medication [like the case -1] as described in Case-I above for one month.

i) [Upto] During nine months of observation, they did not have [nay] any asthmatic [attach,] attacks,

ii) No shortness of [breathing] breath was reported by them,

iii) In the case of the male patient, his [was] smoking was a risk enhancer [of the frequent episode of] for an asthmatic attack. [But] However, he did not have any breathing discomfort [for] due to smoking even exceeding [the] his regular schedule.

iv) The f[F]emale patient had shortness of [breathing] breath when she took long walks or [climbing of the stair cases only upto a single floor] climbed even a single staircase, but during treatment, she did not have any trouble [of] breathing even when she climbed [upto] up to the third level.

IN THE CLAIMS:

Claims 1-12, 18, 19 and 39 have been cancelled.

The claims have been amended as follows:

13. (Amended) Pharmaceutical composition useful in the treatment of asthma, said composition comprising an [effective] amount of an extract obtained from the plant *Murraya koenigii* effective for treating asthma together [with, or optionally associated] with [a] at least one pharmaceutically acceptable additive.

14. (Amended) [A] The composition as claimed in claim 13, wherein the at least one [additives] additive [comprise] is a powder or [extracts] extract of at least one [plants] plant selected from the group consisting of *M. paniculate Linn, H. abelmoschus, T. ammi, S. aromaticum, A.vasica Nees,* and *E. hirta*[, and *M. koinegii*].

15. (Amended) [A] The composition as claimed in claim 13, wherein the composition comprises [additives are present in the range of] 80-100 mg of *M. paniculate Linn,* 40-60 mg of *H. abelmoschus,* 38-62 mg of *T. ammi,* 7-13 mg of *S. aromaticum,* 85 - 115 mg of *A.vasica Nees* and 90-110 mg of *E. hirta*.

16. (Amended) [A] The composition as claimed in claim 13, comprising:

M. paniculata Linn. Syn. M. exotica (KAMINI)	90mg
H. abelmoschus (JOWAN)	50mg
T. ammi (LAVANGA)	50mg
S. aromaticum (BASAK)	10mg
A.vasica Nees (PUSITOA)	100mg
E.hirta	100mg
M. koinegii (Suravi Neem)	100mg.

17. (Amended) [A] The composition as claimed in claim 13, wherein the extract of the plant *M. [koinegii]* koenegii is present in the range of 87-105 mg per dose.

20. (Amended) [A] The composition as claimed in claim 13, wherein the extract has active principles [have] having R_f values 0.73, 0.60, [034] 0.34 and 0.14 in chloroform and methanol in the ratio 19:1 and R_f values 0.60, 0.38, [024] 0.24 and 0.15 in [the] chloroform.

21. (Amended) [A] The composition as claimed in claim 13, wherein the extract exhibits four peaks having retention times of 3.37, 3.49, 4.0 and 5.69 minutes in high pressure liquid chromatography over octyl decyl silane medium using methanol solvent and detection of absorbance at 254 nm [having four peak with retention time 3.37, 3.49, 4.0 and 5.69 in methanol as solvent at 254nm].

22. (Amended) [A] The composition as claimed in claim 13, wherein the extract obtained from the plant *M. [koinegii] koenegii* exhibits antioxidant [property i.e. O_2 inhibition] activity.

24. (Amended) [A] The method as claimed in claim 23, wherein the lyophilized extract obtained from *Murraya [Koenigii] koenigii* is administered along with [other conventional] at least one pharmaceutically acceptable [additives] additive for the treatment of asthma.

25. (Amended) [A] The method as claimed in claim 23, wherein the mode of administration is oral for the treatment of mild or acute asthma.

26. (Amended) [A] The method as claimed in claim 23, wherein the dosage level of the composition is in between 325-600 mg twice daily for the period ranging from 3 to 30 days.

27. (Amended) [A] The method as claimed in claim 23, wherein the dosage level is in between 325-600 mg twice daily for the period ranging from 3 to 15 days for mild asthmatic condition[, and 15 - 30 days for acute asthmatic condition].

28. (Amended) [A] The method as claimed in claim [23] 24, wherein the [additives] additive [are] is at least one selected from the group consisting of *M. paniculate Linn*, *H. abelmoschus*, *T. ammi*, *S. aromaticum*, *A.vasica Nees* and *E. hirta*[, and *M. koinegii*].

29. (Amended) [A] The method as claimed in claim [23] 28, [where in] wherein the [additives are present in a range of] composition comprises 80-100 mg of *M. paniculate Linn*, 40-60 mg of *H. abelmoschus*, 38-62 mg of *T. ammi*, 7-13 mg of *S. aromaticum*, 85-115 mg of *A.vasica Nees*, 90-110 mg of *E. hirta*, along with[, and] 87-105 mg of *M.* [*koinegii*.] *koenegii* per dose.

30. (Amended) [A] The method as claimed in claim [23] 29, wherein the [additives are preferably present in an amount] composition comprises 90 mg of *M. paniculate Linn*, 50 mg of *H. abelmoschus*, 50 mg of *T. ammi*, 10 mg of *S. aromaticum*, 100 mg of *A.vasica Nees*, 100 mg of *E hirta*, along with [and] 100 mg of *M.* [*koinegii.*] *koenegii* per dose.

31. (Amended) [A] The method as claimed in claim [23] 24, wherein the composition comprises the additives *M. paniculate Linn*, *H. abelmoschus*, *T. ammi*, *S. aromaticum*, *A.vasica Nees*, *E. hirta*, [and *M. koinegii* are administered to include properties such] and is also effective as an [antidiahorial] antidiarrheal, antiseptic, carminative, [stimulation] stimulant, [anti-cough] antitussive, anti- bronchitis agent and for nourishment.

32. (Amended) [A] The method as claimed in claim [23] 28, wherein the additives are obtained from :
bark or root of *M. paniculate Linn*; [(bark or root),] dried flower buds of *H. abelmoschus*; [from dried flower buds,] leaves of *T. ammi*; [from leaves] whole plant parts of *S. aromaticum*; [from whole plant] root of *A.vasica Nees* [from root,] and bark of *E. hirta* [from bark, and *M. konegii* from leaves].

33. (Amended) An anti-oxidant composition for human beings and animals, said composition comprising an effective amount of an extract obtained from the plant *Murraya [Koenigii]* koenigii

[together with or] and optionally[, associated with] at least one pharmaceutically acceptable [additives] additive.

34. (Amended) [A] The composition as claimed in claim 33, wherein at least one [additives] additive [comprise] is present in the composition and is a powder or [extracts] extract of at least one [plants] plant selected from the group consisting of *M. paniculate Linn*, *H. abelmoschus*, *T. ammi*, *S. aromaticum*, *A.vasica Nees* and *E. hirta*[, and *M. koinegii*].

35. (Amended) [A] The composition as claimed in claim [33] 34, wherein the composition comprises [additives are present in a range of] 80-100 mg of *M. paniculate Linn*, 40-60 mg of *H. abelmoschus*, 38-62 mg of *T.ammi*, 7-13 mg of *S. aromaticum*, 85-115 mg of *A.vasica Nees*, 90-110 mg of *E. hirta*, along with [and] 87-105 mg of *M. [koinegii.] koenegii* per dose.

36. (Amended) [A] The composition as claimed in claim [33] 35, [where in] wherein the composition comprises [additives are preferably present in an amount] 90 mg of *M. paniculate Linn*, 50 mg of *H. abelmoschus*, 50 mg of *T. ammi*, 10 mg of *S. aromaticum*, 100 mg of *A.vasica Nees*, 100 mg of *E. hirta*, along with [and] 100 mg of *M. [koinegii.] koenegii* per dose.

37. (Amended) [A] The composition as claimed in claim [33] 34, wherein the additives *M. paniculate Linn*, *H. abelmoschus*, *T.*

ammi, S. aromaticum, A.vasica Nees, E. hirta along with [and] *M. [koinegii] koenegii* are used as [are added to provide properties namely,] an [antidiahorial] antidiarrheal, antiseptic, carminative, [stimulation] stimulant, [anti-cough] antitussive, anti- bronchitis agent and nourishment, respectively.

38. (Amended) [A] The composition as claimed in claim [33] 34, wherein the additives are selected from *M. paniculate Linn, H. abelmoschus, T. ammi, S. aromaticum, A.vasica Nees* and *E. hirta,* [and *M. koinegii*] in the form of bark or root; seed; fruit; dried flower buds; leaves; whole plant; and root and bark, [leaves,] respectively.

Claims 41-52 have been added.